ORIGINAL ARTICLE

UDC: 618.19-006-07
DOI: https://doi.org/10.2298/VSP240606005N

Contrast-enhanced mammography in breast cancer screening: our experiences

Kontrastna mamografija u skriningu karcinoma dojke: naša iskustva

Dijana Nićiforović*†, Marijana Basta Nikolić*†, Zorka Drvendžija†, Olivera Nikolić*†, Aleksandra Mijatović*, Sonja Lukač*, Sanja Stojanović*†

***University Clinical Center of Vojvodina, Center for Radiology, Novi Sad, Serbia;**
†University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia

Abstract

Background/Aim. Breast cancer is a leading global health concern. Contrast-enhanced mammography (CEM) presents a promising advancement in early breast cancer detection, excelling in sensitivity, specificity, and cost-effectiveness. The aim of the study was to assess the overall diagnostic efficacy of CEM in breast cancer screening, particularly in distinguishing benign from malignant lesions in dense breasts. **Methods.** A two-year retrospective study was conducted at the Center for Radiology, including a total of 279 women undergoing CEM following standard mammography. **Results.** CEM demonstrated high sensitivity (92.4%), specificity (75.1%), and a noteworthy negative predictive value of 97.0%, significantly reducing unnecessary biopsies. **Conclusion.** CEM is a valuable screening tool, offering enhanced diagnostic capabilities and the potential to reduce the number of unnecessary biopsies. It is particularly beneficial for patients with dense breasts or inconclusive traditional mammography results.

Key words:
breast cancer; diagnosis; differential diagnosis; mammography; mass screening; sensitivity and specificity; ultrasonography, mammary.

Apstrakt

Uvod/Cilj. Karcinom dojke je vodeći globalni zdravstveni problem. Kontrastna mamografija (KM) koju odlikuje osetljivost, specifičnost i ekonomičnost predstavlja obećavajući napredak u ranom otkrivanju karcinoma dojke. Cilj rada bio je da se utvrdi ukupna dijagnostička efikasnost KM u skriningu karcinoma dojke, posebno u razlikovanju benignih od malignih lezija dojki čije tkivo je „gusto". **Metode.** Retrospektivnom studijom, sprovedenom tokom dve godine u Centru za radiologiju, obuhvaćeno je 279 žena, kojima je posle standardne mamografije urađena KM. **Rezultati.** Primenom KM utvrđeni su visoka osetljivost (92,4%), specifičnost (75,1%) i značajna negativna prediktivna vrednost od 97,0%, što je značajno smanjilo broj nepotrebnih biopsija. **Zaključak.** KM je dragocena alatka za skrining, koja omogućava poboljšane dijagnostičke mogućnosti i potencijal da se smanji broj nepotrebnih biopsija. Posebno je korisna za bolesnice čije dojke imaju „gusto" tkivo ili kod neuverljivih rezultata tradicionalne mamografije.

Ključne reči:
dojka, neoplazme; dijagnoza; dijagnoza, diferencijalna; skrining; senzitivnost i specifičnost; ultrasonografija, dojka.

Introduction

Breast cancer (BC) is a leading cause of cancer-related death among women globally. It presents a significant challenge in early detection and treatment and remains one of the most prevalent cancers worldwide, significantly affecting women's health across all demographics. According to the World Health Organization (WHO), BC accounts for approximately 12% of all new annual cancer cases globally [1]. The American Cancer Society reports that in the United States alone, an estimated 287,850 new cases of invasive BC were expected to be diagnosed in women in 2021, alongside 51,400 new cases of non-invasive (*in situ*) BC [2]. These statistics highlight the widespread nature of this disease and the critical importance of early detection and effective treatment strategies. The five-year relative survival rate for localized BC is 99%. However, this rate drops to 86% for regional spread (to nearby structures or lymph nodes) and plummets to 28% for distant spread (metastasized cancer) [3]. These figures underscore the urgent need for access to early treatment and advancements in diagnostic technologies, such as contrast-enhanced mammography (CEM), to improve early detection rates, particularly in

Correspondence to: Dijana Nićiforović, University of Novi Sad, Faculty of Medicine, Hajduk Veljkova 3, 21 000 Novi Sad, Serbia.
E-mail: dijana.niciforovic@mf.uns.ac.rs

populations at higher risk, including those women with dense breast (DB) tissue.

Traditional mammography has been the cornerstone of BC screening for decades, significantly contributing to reduced mortality rates through early detection. However, its sensitivity is compromised in women with DB tissue, where the fibroglandular tissue can obscure cancerous lesions, leading to a higher rate of missed diagnoses [4]. Despite its widespread use, the limitations of mammography highlight the need for complementary or alternative imaging techniques to enhance detection rates, especially in this subgroup of patients. While breast ultrasound (US) is frequently used as an adjunct to mammography, increasing the detection rate of BCs, particularly in DBs, it also has a higher false-positive rate, leading to more frequent and often unnecessary biopsies [5].

Breast magnetic resonance imaging (MRI) offers high sensitivity and is particularly useful for screening high-risk populations and assessing the extent of disease in known cancer cases. Its ability to provide detailed images without ionizing radiation is a significant advantage. However, the high cost, limited availability, and contraindications for some patients (e.g., those with certain implants or claustrophobia) restrict its routine use in the general population [6].

CEM represents a significant advancement in breast imaging technology, offering enhanced diagnostic capabilities, particularly in DB tissue [7]. CEM utilizes a dual-energy imaging technique performed after the intravenous administration of an iodinated contrast agent [8]. The process involves acquiring low- and high-energy images in rapid succession: the low-energy images are comparable to standard mammography, while the high-energy images are more sensitive to the contrast agent [9]. This dual-energy approach allows radiologists to isolate and highlight areas with increased contrast uptake, typically indicative of malignant tissue due to higher blood supply [10].

CEM has demonstrated its utility in detecting cancers not visible on standard mammograms, distinguishing benign from malignant lesions, and ultimately reducing unnecessary biopsies [11]. Besides detecting cancers in DBs and high-risk patients, another important indication for CEM is its use in the preoperative assessment of known BC to determine accurately the extent of disease. CEM has proven effective in identifying multifocal, multicentric, and contralateral diseases, which are critical factors in treatment planning [12]. Additionally, CEM is useful in monitoring responses to neoadjuvant chemotherapy, allowing clinicians to assess tumor response and residual disease, influencing surgical decisions and further treatment planning [11].

Compared to traditional digital mammography (DM), CEM offers superior sensitivity and specificity, especially in DB tissue. This is crucial for early BC detection, leading to potentially better treatment outcomes [13]. It also aids in differentiating benign from malignant lesions, which can reduce unnecessary procedures and patient anxiety [14]. Compared to breast MRI, CEM is more cost-effective, widely accessible, and less time-consuming, making it an attractive alternative in many healthcare settings [12]. Both CEM and breast MRI play vital roles in BC imaging. MRI remains the gold standard for screening high-risk populations and evaluating DB tissue, offering unparalleled sensitivity for detecting small lesions, especially in women with DBs. However, MRI can be more expensive and less widely available than CEM and requires more time and specialized equipment.

While it involves radiation exposure, CEM is faster, more cost-effective, and widely available. It has been shown to have higher specificity than breast MRI, reducing the likelihood of false positives and unnecessary biopsies [15]. Moreover, CEM can be more comfortable for patients since it does not require the prolonged prone positioning and confinement associated with MRI. In patients who cannot undergo MRI due to contraindications, such as claustrophobia, the presence of certain implants, or limited availability, CEM can serve as a valuable alternative [16].

Despite its many advantages, CEM does come with limitations. While it involves additional radiation exposure compared to standard mammography, the risk is generally considered low, though it remains a factor for patients requiring frequent imaging [8]. Using iodinated contrast agents can cause allergic reactions in some individuals, though severe reactions are rare [17]. Furthermore, CEM requires specialized equipment and trained personnel, and its accessibility can be limited in certain regions due to the costs involved [18]. Patients with impaired renal function are at higher risk for nephropathy, given the use of iodinated contrast agents [19].

The aim of the study was to assess the capability of CEM in decreasing the frequency of biopsies following screening recalls and to evaluate the overall diagnostic value of CEM in BC screening.

Methods

This retrospective study was conducted at the Center for Radiology, University Clinical Center of Vojvodina, Serbia, between December 2021 and December 2023. The study included 279 women who underwent CEM following standard 2D mammography. The study was approved by the Ethics Committee of the University Clinical Center of Vojvodina (No. 00–43, February 9, 2024). Participants were selected based on their recall from the initial national and opportune screening mammography, indicating the need for further evaluation. All CEM procedures were performed using the Hologic Selenia® Dimensions® 3D machine. Standard protocol in image acquisition was followed: after a standard 2D mammography in mediolateral oblique and craniocaudal projections of both breasts, which urged further workup, CEM was performed in all patients, with intravenous application of a low-osmolarity iodine-based contrast material (Omnipaque™) in the total volume of 1.5 mL/kg of body weight (not more than 150 mL) with the use of an injector, with an injection rate of 2–3 mL/sec, followed by a saline flush. Image acquisition began about 2–2.5 min after contrast material injection, in standard craniocaudal and mediolateral views, first of the symptomatic breast, followed by the presumably healthy breast. Both low- and high-energy images were obtained in quick succession while the breast remained compressed. The whole image acquisition process lasted for approximately 6 to 7 min in total. The images were described using Breast Imaging Reporting & Data System (BI-RADS)

classification, with results BI-RADS ≥ 3 considered positive and BI-RADS < 3 negative. Participants initially underwent standard 2D mammography. Based on these results, CEM was performed for further assessment. In cases where CEM indicated potential malignancies, patients were referred for biopsy. Core biopsy was the method of choice whenever we visualized the lesion. If that was not the case, the patient was transferred to vacuum-assisted biopsy. Eventually, all the patients were graded based on BI-RADS. The primary outcomes set for the study were the detection rate of BC using CEM and the reduction in biopsy rates post-CEM.

Statistical analysis

Statistical analyses were performed to compare the diagnostic efficacy of CEM against traditional methods and to evaluate the impact of CEM on the decision-making process regarding biopsies. From statistical analyses, we utilized cross-tabulation, binary logistic regression, and receiver operating characteristic (ROC) analysis, and determined sensitivity, specificity, and negative predictive value.

Results

A total of 279 women who underwent CEM, standard mammography, and US were analyzed. The average age of all participants was 59 years, with the oldest one being 81 years old and the youngest 40 years old.

The mammography findings were pathological (BI-RADS ≥ 3) in 249 women. A BI-RADS score of 2 was found in 30 women, but due to having DBs, they were referred to additional breast US. US findings were pathological (BI-RADS ≥ 3) in 150 women, while the remaining 129 women had normal results (Figure 1).

Due to insufficient agreement between mammographic and US findings and the need to determine whether biopsies were truly necessary for changes characterized by BI-RADS ≥ 4, CEM was performed in all 279 patients. Among them, 114 exhibited changes in CEM that raised suspicion of malignant alterations, while 165 women had normal CEM findings (negative CEM, BI-RADS < 3). Employing CEM in these patients prevented unnecessary biopsies that would otherwise be indicated by mammography or US (Figure 1). Out of the 114 patients with positive CEM findings, biopsies were conducted for 107 patients. For seven patients with BI-RADS 3 lesions, radiologists opted for monitoring and follow-up after three months. Core biopsy was performed in 86 women and vacuum-assisted biopsy in 23, with both biopsies conducted for two patients.

All patients with negative CEM were followed up on six-month intervals and showed stability of findings. Histopathological findings revealed that 66 women had malignant changes, while 41 biopsied patients had benign changes. This determined that out of a total of 279 women, 66 had BC, and 213 had benign findings on the breasts (Table 1).

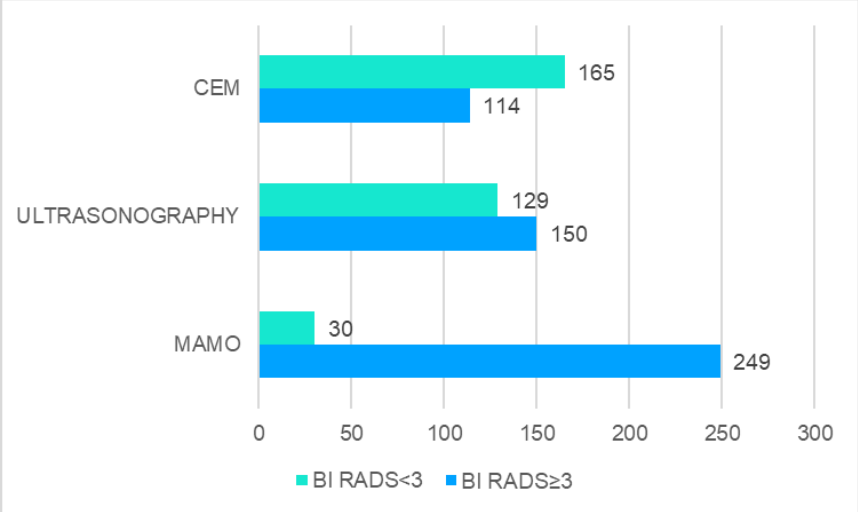

Fig. 1 – Structure of the examined group based on radiological imaging results. MAMO – mammography; CEM – contrast-enhanced mammography; BI-RADS – Brest Imaging Reporting Data System ≥ 3 considered positive; BI-RADS < 3 considered negative. All values are given as numbers.

Table 1

Correlation between breast findings (based on pathohistological and radiological imaging) and CEM findings

Parameter	BC	BBF	Total
CEM positive	61	53	114
CEM negative	5	160	165
Total	66	213	279

CEM – contrast-enhanced mammography; BC – breast cancer; BBF – breast benign finding.
All values are given as numbers.

Out of the 114 women with positive CEM results, 61 were confirmed to have cancer (Table 1). However, 5 patients with cancer had normal CEM findings because they had ductal carcinoma *in situ*, presented as microcalcifications, with no enhancement on CEM or subtle enhancement that was misinterpreted as BC.

The sensitivity of CEM was 92.42%, specificity was 75.11%, positive predictive value (PPV) was 53.51%, and negative predictive value (NPV) was 96.97% (Table 2).

According to binary logistic regression results, significant predictors for the presence of BC were CEM, US, and age, with CEM being the strongest predictor. Conventional mammography findings were not statistically significant (Table 3). Persons with a positive CEM result were 60 times more likely to have BC than those with a negative CEM result (Exp(B) = 60.07). Through ROC analysis, we determined that, in terms of age, the cut-off value for the occurrence of BC was 55.50 years (Table 4, Figure 2).

Table 2

Diagnostic performance of CEM in detecting breast cancer

Measure	Value (%)
Sensitivity	92.42
Specificity	75.11
PPV	53.51
NPV	96.97

CEM – contrast-enhanced mammography; PPV – positive predictive value; NPV – negative predictive value.

Table 3

Prediction of the probability that a patient has breast cancer

Parameter	B	S.E.	Wald	*df*	Sig.	Exp(B)	95% CI for Exp(B)	
							lower	upper
Age	0.09	0.03	12.40	1	0.00	1.09	1.04	1.14
MAMO	1.23	0.84	2.15	1	0.14	3.43	0.66	17.86
US	1.77	0.48	13.60	1	0.00	5.87	2.29	15.03
CEM	4.09	0.65	39.29	1	0.00	60.07	16.69	216.16

MAMO – mammography; US – ultrasound; CEM – contrast-enhanced mammography; CI – confidence interval; Exp(B) – odds ratio.

Table 4

Cut-off value of age for the presence of breast cancer

Parameter	AUC	*p*	Cut-off	Sensitivity	Specificity
Age	0.59	0.03	55.50 years	82.80 %	63.00 %

AUC – area under the curve.

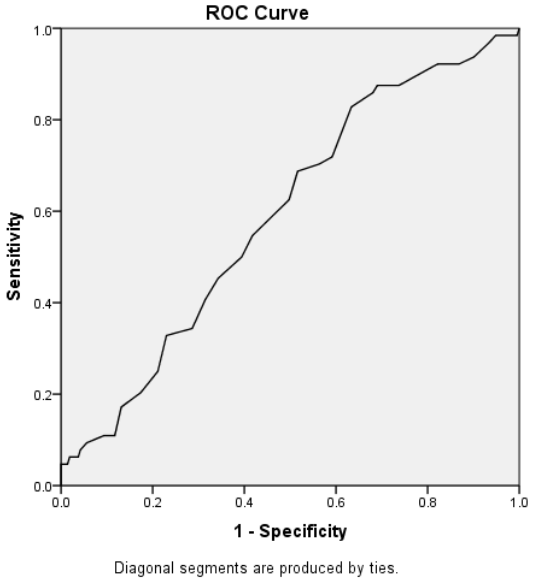

Fig. 2 – Receiver operating characteristic (ROC) curve analysis of age for the presence of breast cancer.

Discussion

The results of our study on the diagnostic performance of CEM in BC screening provide significant insights, particularly when compared to traditional mammography methods. Our findings indicate a high sensitivity (92.42%) and a reasonable specificity (75.11%) for CEM, alongside a PPV of 53.51% and an NPV of 96.97%. It is similar to the recent study showing a 95.4% sensitivity in cancer detection using CEM [20]. Additionally, the authors of the mentioned article also highlight the positive correlation between the intensity of the *post*-contrast enhancement of the suspicious lesion and the aggressiveness of the malignant process, which our study did not include but is a very interesting perspective worth further investigation.

Some authors state that CEM adoption is simple, especially for radiologists experienced in DM and MRI [12, 21]. The study published by Cheung et al. [13] states that an average of 75 CEM readings is sufficient for reaching a 90% probability of correct prediction.

This increased sensitivity is crucial in the context of BC screening, as it implies a greater likelihood of detecting cancer, especially in its early stages (Figures 3 and 4). The increased specificity of CEM also makes it a valuable tool in screening, particularly for DB tissues where mammography often falls short, mainly because of its ability to provide additional vascular imaging [22]. In a study involving 89 women with DBs and 100 lesions, CEM, in addition to mammography, showed improved sensitivity from 71.5% to 92.7%, along with specificity from 51.8% to 67.9% [13]. Another study reported that out of 14 cancers, CEM detected 13 (93%) cancers that were not seen at full-field DM in women with DBs [11]. Our study comprised only inconclusive mammographies that required additional work, and, therefore, we did not calculate the diagnostic performance of DM alone, as we assumed that these data would show unrealistic and incorrectly low sensitivity and specificity of DM alone. In this scenario in our study, DM findings were not statistically significant predictors for BC. The role of US in BC detection, especially in DBs, has been well documented [23]. Meta-analysis of 526 studies by Sood et al. [24] showed that US had

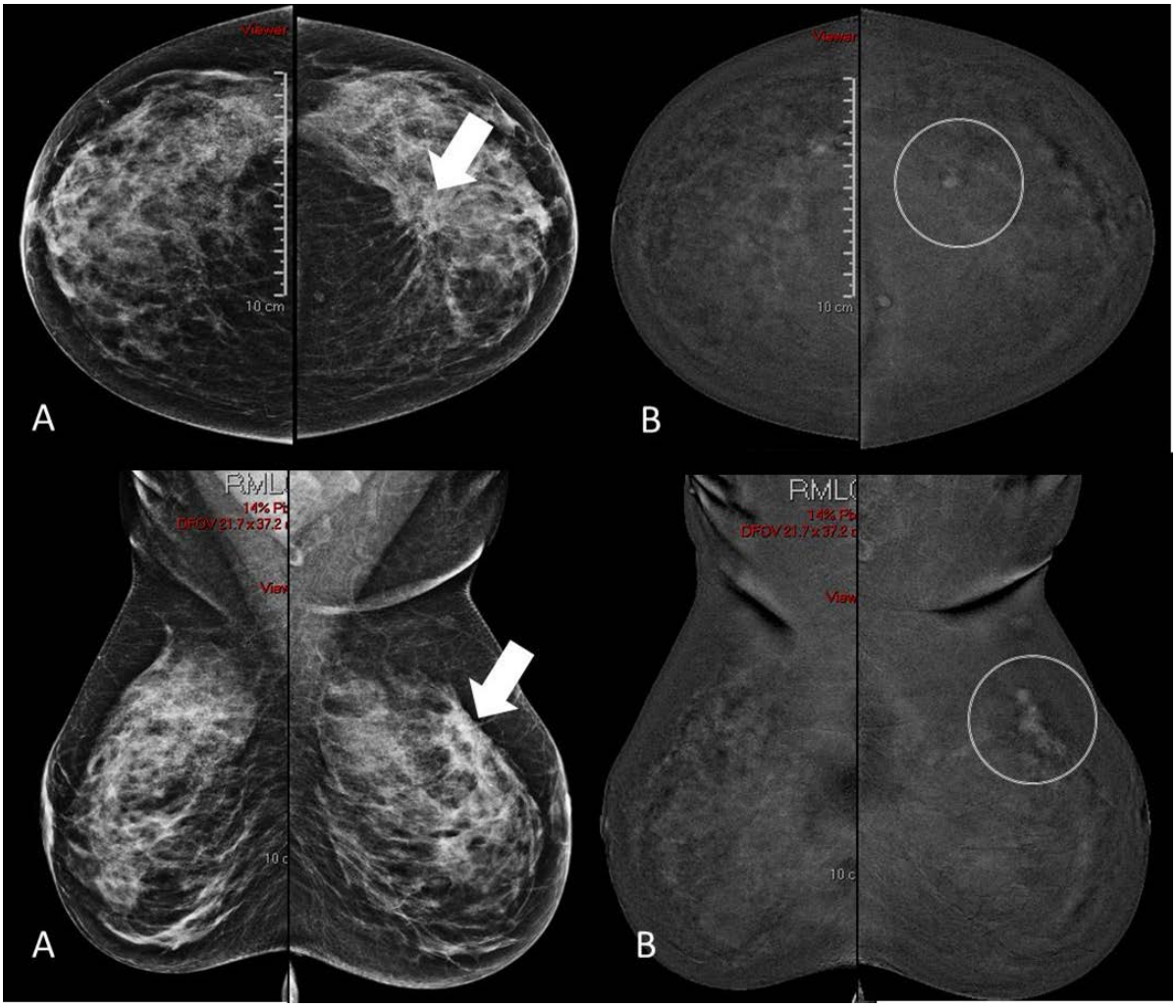

Fig. 3 – Digital mammography demonstrates architectural distortion at the junction of the upper quadrants of the left breast (white arrow) (A), which shows intense post-contrast enhancement on contrast-enhanced mammographic images (marked by white circle) (B). Histopathology following biopsy confirmed invasive lobular cancer grade 2.

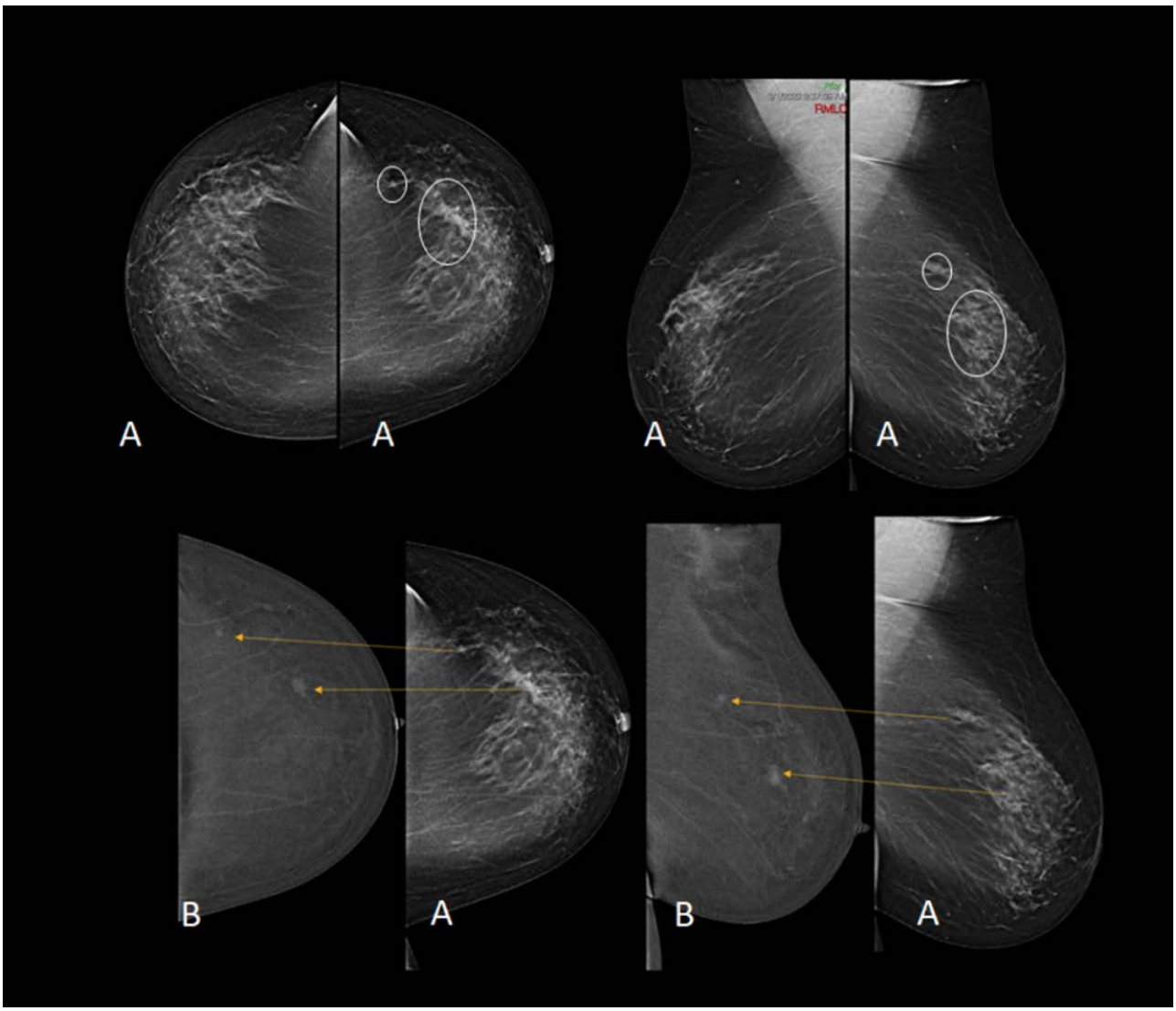

Fig. 4 – A) Digital mammography with tomosynthesis demonstrates architectural distortion in the upper lateral quadrant of the left breast, not depictable by ultrasound. A zone of focal asymmetry is also present in the axillary tail of the same breast (marked by a circle). B) Contrast-enhanced mammography demonstrates contract enhancement of both mammographically detected lesions (yellow arrows). Since the lesions were not visualized by ultrasound, a vacuum-assisted biopsy was performed confirming invasive ductal breast cancer no special type grade 2.

an overall pooled sensitivity, specificity, diagnostic odds ratio, PPV, and NPV (95% confidence interval – CI) of 80.1%, 88.4%, 30.7, 0.86, and 0.80, respectively, for the detection of BC. It is particularly beneficial as an adjunct to mammography for evaluating palpable abnormalities and clarifying indeterminate mammographic findings. US excels in differentiating solid from cystic masses and has proven effective in further investigating areas of concern detected on mammograms [25].

However, US also presents challenges, notably its operator-dependent nature, which can lead to variability in diagnostic performance. Its higher false-positive rate can lead to additional follow-up tests and biopsies, which may not be necessary with more definitive imaging techniques like CEM [26]. Our study showed increased sensitivity of CEM compared to US (92.42%), somewhat lower specificity of 75.11%, and PPV of 53.51%. The most significant advantage of CEM compared to US is the high NPV of 96.97%, which grants high confidence that no cancer is present when CEM is negative, thus allowing a significant decrease in follow-up and biopsy rates.

A study conducted in Korea highlighted that approximately 90% of cancers were detected using CEM, which was just marginally lower than MRI. Furthermore, the visibility of the tumor was superior using CEM compared with full-field DM or digital tomosynthesis for US-detected BCs [27].

Several studies have demonstrated a similar diagnostic performance of CEM to breast MRI along with other advantages, such as lower costs, the possibility of upgrading existing DM units, broader availability, and fewer contraindications [28]. In addition, a shorter learning curve, higher specificity, and NPV compared to breast MRI make CEM a solution tool for inconclusive findings on screening mammography limited by glandular density [29].

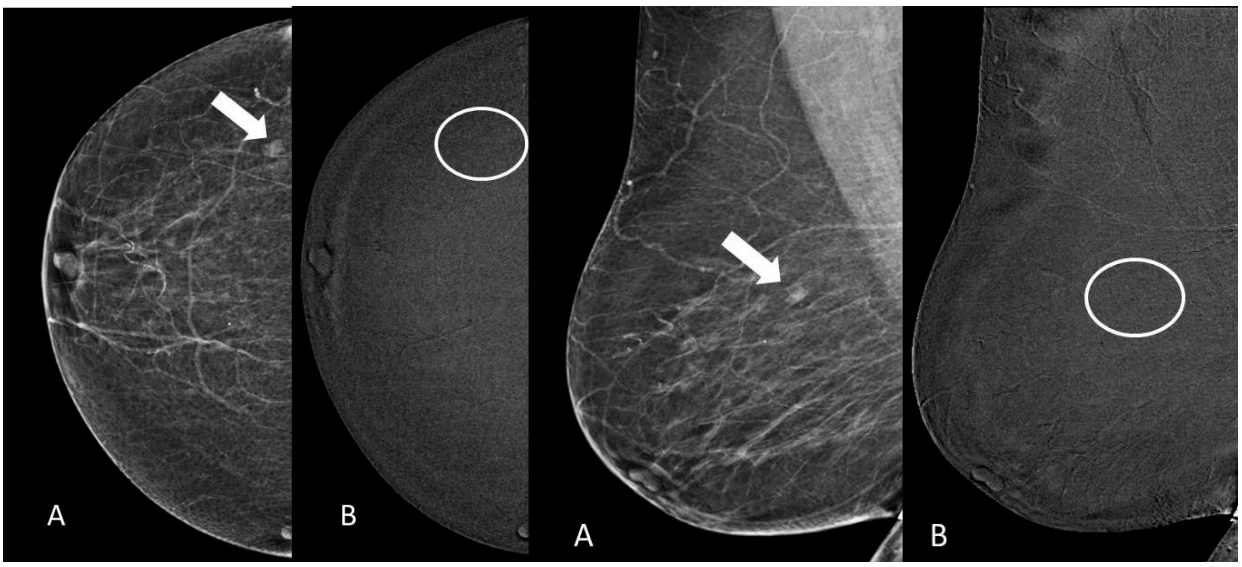

Fig. 5 – Digital mammography with tomosynthesis demonstrates a small lesion, with lobulated, somewhat indistinct margins in the upper lateral quadrant of the right breast (white arrow) (A). The lesion shows no enhancement on contrast-enhanced mammography (depicted by a white circle) (B), thus follow-up was recommended instead of the biopsy. The lesion remained stable on a 6-month follow-up examination.

In institutions like ours, lacking dedicated MRI-guided biopsy tools, CEM emerges as a valuable alternative that showcases superiority over traditional MRI for biopsy procedures. This inherent adaptability positions CEM as an efficient and pragmatic choice for biopsy procedures in settings without MRI-guided biopsy capabilities, providing a reliable and accessible solution for targeted tissue sampling in breast diagnostics [29].

This high NPV of 96.97% suggests that patients can be reassured with a high degree of confidence when CEM indicates no cancer. This aspect of CEM can be a significant advantage in clinical practice, reducing patient anxiety and the need for unnecessary biopsies [30, 31]. However, in our study, five patients with later proven cancer had negative CEM. In all five cases, histopathology confirmed pure ductal carcinoma *in situ*, which, according to the known data [32, 33], usually shows non-mass contrast enhancement but, in certain cases, may show no enhancement at all.

Our study highlighted the potential of CEM to reduce unnecessary biopsies. With 62.5% of women avoiding biopsies based on CEM findings (in 23 of them vacuum-assisted biopsy was performed), there is a clear indication that CEM can effectively discriminate between benign and malignant lesions (Figure 5). This reduction in biopsy rates is not only beneficial in terms of patient comfort and reducing healthcare costs but also in minimizing the risk of complications associated with invasive procedures. A recent prospective study observed a potential 16.4% net reduction of the biopsy rate that could be obtained using CEM [31].

Although the average age of all participants in our study was 59 years, based on the ROC curve analysis results, we observed that the cut-off value for the presence of BC was 55.5 years. This indicates a need for caution with women of this age group in our population and may facilitate easier decision-making regarding CEM, provided clear indications exist.

Conclusion

Our study supports the growing body of evidence that contrast-enhanced mammography is a valuable tool in breast cancer screening, offering high sensitivity and the potential to reduce unnecessary biopsies, together with significant performance simplicity and patient acceptance. As breast cancer screening continues to evolve, contrast-enhanced mammography stands out as a promising technology, particularly for patients with dense breast tissue or inconclusive traditional mammography results.

REFERENCES

1. *World Health Organization.* Breast Cancer [Internet]. Geneva: WHO; 2024 [accessed 2024, Dec 2]. Available from: https://www.who.int/news-room/fact-sheets/detail/breast-cancer
2. *American Cancer Society.* Breast Cancer Facts & Figures 2022–2024 [Internet]. Atlanta: American Cancer Society, Inc. 2022. [cited on 2024 May 10; accessed 2024 Dec 9]. Available from: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/2022-2024-breast-cancer-fact-figures-acs.pdf
3. *Siegel RL, Miller KD, Fuchs HE, Jemal A.* Cancer Statistics, 2021. CA Cancer J Clin 2021; 71(1): 7–33. Erratum in: CA Cancer J Clin 2021; 71(4): 359.
4. *Boyd NF, Guo H, Martin LJ, Sun L, Stone J, Fishell E,* et al. Mammographic density and the risk and detection of breast cancer. N Engl J Med 2007; 356(3): 227–36.
5. *Corsetti V, Houssami N, Ferrari A, Ghirardi M, Bellarosa S, Angelini O,* et al. Breast screening with ultrasound in women with mammography-negative dense breasts: evidence on incremen-

tal cancer detection and false positives, and associated cost. Eur J Cancer 2008; 44(4): 539–44.
6. *Lehman CD, Lee JM, DeMartini WB, Hippe DS, Rendi MH, Kalish G,* et al. Screening MRI in women with a personal history of breast cancer. J Natl Cancer Inst 2016; 108(3): djv349.
7. *Perry H, Phillips J, Dialani V, Slanetz PJ, Fein-Zachary VJ, Karimova EJ,* et al. Contrast-enhanced mammography: A systematic guide to interpretation and reporting. AJR Am J Roentgenol 2019; 212(1): 222–31.
8. *Jochelson MS, Dershaw DD, Sung JS, Heerdt AS, Thornton C, Moskowitz CS,* et al. Bilateral contrast-enhanced dual-energy digital mammography: feasibility and comparison with conventional digital mammography and MR imaging in women with known breast carcinoma. Radiology 2012; 266(3): 743–51.
9. *Lewin JM, Isaacs PK, Vance V, Larke FJ.* Dual-energy contrast-enhanced digital mammography: feasibility. Radiology 2003; 229(1): 261–8.
10. *Elder K, Matheson J, Nickson C, Box G, Ellis J, Mou A,* et al. Contrast enhanced mammography in breast cancer surveillance. Breast Cancer Res Treat 2023; 199(2): 221–30.
11. *Fallenberg EM, Dromain C, Diekmann F, Renz DM, Amer H, Ingold-Heppner B,* et al. Contrast-enhanced spectral mammography: Does mammography provide additional clinical benefits or can some radiation exposure be avoided? Breast Cancer Res Treat 2014; 146(2): 371–81.
12. *Lawson MB, Partridge SC, Hippe DS, Rahbar H, Lam DL, Lee CI,* et al. Comparative Performance of Contrast-enhanced Mammography, Abbreviated Breast MRI, and Standard Breast MRI for Breast Cancer Screening. Radiology 2023; 308(2): e230576.
13. *Cheung YC, Lin YC, Wan YL, Yeow KM, Huang PC, Lo YF,* et al. Diagnostic performance of dual-energy contrast-enhanced subtracted mammography in dense breasts compared to mammography alone: interobserver blind-reading analysis. Eur Radiol 2014; 24(10): 2394–403.
14. *Ghaderi KF, Phillips J, Perry H, Lotfi P, Mehta T.* Contrast-enhanced Mammography: Current Applications and Future Directions. Radiographics 2019; 39(7): 1907–20.
15. *Jong RA, Yaffe MJ, Skarpathiotakis M, Shumak RS, Danjoux NM, Gunesekara A,* et al. Contrast-enhanced digital mammography: initial clinical experience. Radiology 2003; 228(3): 842–50.
16. *Lobbes MB, Smidt ML, Houwers J, Tjan-Heijnen VC, Wildberger JE.* Contrast-enhanced mammography: techniques, current results, and potential indications. Clin Radiol 2013; 68(9): 935–44.
17. *Chiu TM, Chu SY.* Hypersensitivity Reactions to Iodinated Contrast Media. Biomedicines 2022; 10(5): 1036.
18. *Neeter LMFH, Raat HPJF, Alcantara R, Robbe Q, Smidt ML, Wildberger JE,* et al. Contrast-enhanced mammography: what the radiologist needs to know. BJR Open 2021; 3(1): 20210034.
19. *McDonald RJ, McDonald JS, Bida JP, Carter RE, Fleming CJ, Misra S,* et al. Intravenous contrast material-induced nephropathy: causal or coincident phenomenon? Radiology 2013; 267(1): 106–18. Erratum in: Radiology 2016; 278(1): 306.
20. *Marzogi A, Baltzer PAT, Kapetas P, Milos RI, Bernathova M, Helbich TH,* et al. Is the Level of Contrast Enhancement on Contrast-Enhanced Mammography (CEM) Associated with the Presence and Biological Aggressiveness of Breast Cancer? Diagnostics 2023; 13(4): 754.
21. *Jochelson MS, Lobbes MBI.* Contrast-enhanced Mammography: State of the Art. Radiology 2021; 299(1): 36–48.
22. *Moffa G, Galati F, Maroncelli R, Rizzo V, Cicciarelli F, Pasculli M,* et al. Diagnostic Performance of Contrast-Enhanced Digital Mammography versus Conventional Imaging in Women with Dense Breasts. Diagnostics (Basel) 2023; 13(15): 2520.
23. *Catalano O, Fusco R, De Muzio F, Simonetti I, Palumbo P, Bruno F,* et al. Recent Advances in Ultrasound Breast Imaging: From Industry to Clinical Practice. Diagnostics (Basel) 2023; 13(5): 980.
24. *Sood R, Rositch AF, Shakoor D, Ambinder E, Pool KL, Pollack E,* et al. Ultrasound for Breast Cancer Detection Globally: A Systematic Review and Meta-Analysis. J Glob Oncol 2019; 5: 1–17.
25. *Berg WA, Gutierrez L, NessAiver MS, Carter WB, Bhargavan M, Lewis RS,* et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. Radiology 2004; 233(3): 830–49.
26. *Tagliafico AS, Calabrese M, Mariscotti G, Durando M, Tosto S, Monetti F,* et al. Adjunct Screening With Tomosynthesis or Ultrasound in Women With Mammography-Negative Dense Breasts: Interim Report of a Prospective Comparative Trial. J Clin Oncol 2016; 34(16): 1882−88.
27. *Youn I, Choi S, Choi YJ, Moon JH, Park HJ, Ham SY,* et al. Contrast enhanced digital mammography versus magnetic resonance imaging for accurate measurement of the size of breast cancer. Br J Radiol 2019; 92(1098): 20180929.
28. *Sammarra M, Piccolo CL, Sarli M, Stefanucci R, Tommasiello M, Orsaria P,* et al. Contrast-Enhanced Mammography-Guided Biopsy: Preliminary Results of a Single-Center Retrospective Experience. J Clin Med 2024; 13(4): 933.
29. *Cozzi A, Magni V, Zanardo M, Schiaffino S, Sardanelli F.* Contrast-enhanced Mammography: A Systematic Review and Meta-Analysis of Diagnostic Performance. Radiology 2022; 302(3): 568–81.
30. *Nicosia L, Bozzini AC, Pesapane F, Rotili A, Marinucci I, Signorelli G,* et al. Breast Digital Tomosynthesis versus Contrast-Enhanced Mammography: Comparison of Diagnostic Application and Radiation Dose in a Screening Setting. Cancers (Basel) 2023; 15(9): 2413.
31. *Cozzi A, Schiaffino S, Fanizza M, Magni V, Menicagli L, Monaco CG,* et al. Contrast- enhanced mammography for the assessment of screening recalls: a two-centre study. Eur Radiol 2022; 32(11): 7388–99.
32. *Vignoli C, Bicchierai G, De Benedetto D, Boeri C, Vanzi E, Miele V,* et al. Role of preoperative breast dual-energy contrast-enhanced digital mammography in ductal carcinoma in situ. Breast J 2019; 25(5): 1034–6.
33. *Cheung YC, Juan YH, Lin YC, Lo YF, Tsai HP, Ueng SH,* et al. Dual-Energy Contrast-Enhanced Spectral Mammography: Enhancement Analysis on BI-RADS 4 Non-Mass Microcalcifications in Screened Women. PLoS One 2016; 11(9): e0162740.

Received on June 6, 2024
Revised on October 23, 2024
Revised on November 29, 2024
Accepted on December 11, 2024
Online First January 2025